REMARKS

With entry of this amendment, claims 2-17, 19-30 and 39-46 are pending. Reconsideration is requested.

The specification has been amended to correct the spelling of nordihydroguaiaretic, as requested by the Examiner.

Amendment of Claims

Claims 31 – 38 have been canceled without prejudice or disclaimer. Applicants reserve the right to prosecute these canceled claims in another patent application. Claim 18 has also been canceled and the recitation therein has been added to claim 17. Claims 1, 15, 16, 17 have each been amended to recite specific water soluble substituents and to recite "the formula" instead of "a formula," in accordance to the recommendation of the Examiner. The water soluble substituents are supported by the specification at, for example, column 15 line 58 to column 16, line 29. Claim 1 has been rewritten as claim 40 and further been amended to recite "an effective amount of the compound to suppress viral growth," in lieu of "an effective viral growth suppressing amount," to particularly point out the present invention. This amendment is supported throughout the specification, such as, for example, at column 17, lines 41 – 45. Claims 2 and 20 have been amended to recite "NH" instead of "N," also pursuant to the recommendation of the Examiner. Claims 5, 6, 21 and 22 have been amended to recite "the compound" instead of "the substantially purified compound," and "inhibits" instead of "inhibited" as further recommended by the Examiner. Claim 17 has additionally been amended to point out with particularity that the virus "is resistant to acyclovir," as supported by the specification at, for example, column 18, lines 45 – 51. New claims 41-46 have been added as supported by the specification at, for example, columns 11, 12 and 13, Table 3 at column 15 and column 14, lines 59 – 62. No new matter has been added. Entry of these amendments is respectfully requested.

Rejection Under 35 USC §251 for New Matter

The Official Action has rejected claims 1 – 30 and 39 under 35 USC § 251 as being based on new matter. The Official Action asserts that there is no support for the

compound recited in claims 2 and 20 wherein "N" rather than "NH" is recited and wherein the dot in claim 2 is practically illegible and in the wrong position, and further that the nature of this compound "cannot be readily ascertained." (Official Action at page 3) Claims 2 and 20 have been amended to replace "N" with "NH" and the dot size has been enlarged so as to be legible and placed on the line, all as supported in the specification at column 15, line 62, et seq. Accordingly, Applicants request reconsideration and withdrawal of this 35 USC § 251 rejection of claims 2 and 20.

The Official Action has further rejected claims 1 – 30 and 39 on the grounds that "Insertion in the claims of the limitation 'are not . . . CH_3O- and $CH_3(C=O)O$-, simultaneously' does not have support in the prior patent . . . because it neither has literal support in the prior patent by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept . . ." (Official Action at page 3). Applicants respectfully disagree. The subpopulation, in which R_1, R_2, R_3 and R_4 are not CH_3O- simultaneously, is supported by the specification at columns 11, 12 and 13 by the compounds referenced as L1, L2, L3, L4, G1, G2, G3a, G3b, G4a and G4b. For example, referring to the compounds in the specification herein:

L2, also known as 3-O-methyl-NDGA, has the CH_3O- in the 3 position (i.e., R_4 in the present claim 1) (col. 11, line 34);

L3, also known as 4-O-methyl-NDGA has the CH_3O- group in the 4 position (i.e., R_3 in the present claim 1) (col. 11, line 47);

G1 has the CH_3O- group in the 3, 3' and 4 positions (i.e., R_1, R_3 and R_4 in the present claim 1) (col. 12, line 20);

G2 has the CH_3O- group in the 3, 4 and 4' positions (i.e., R_2, R_3 and R_4 in the present claim 1) (col. 12, line 35);

G3a has the CH_3O- group in the R_1 and R_3 positions of the present claim 1 (col. 12, line 55);

G3b has the CH_3O- group in the R_1 and R_4 positions of the present claim 1 (col. 13, line 5);

G4a has the CH_3O- group in the R_2 and R_3 positions of the present claim 1 (col. 13, line 20); and

G4b has the CH_3O- group in the R_2 and R_4 positions of the present claim 1 (col. 13, line 35).

Hence, these structures clearly support a subpopulation of NDGA derivatives in which "R_1, R_2, R_3 and R_4 are not CH_3O- simultaneously."

Similarly, the structures of L4, G3a, G3b, G4a and G4b support a subpopulation of NDGA derivatives in which "R_1, R_2, R_3 and R_4 are not $CH_3(C=O)O$- simultaneously." Nevertheless, claim 1 has been amended and does not contain the language rejected by the Official Action, but claim 40 has been added that contains such language.

In light of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 USC § 251 and favorable consideration of the present claims.

Rejection Under 35 USC § 102(b) anticipated by Jordan (US Patent 4,880,637) in light of Orth et al. (US Patent 5,342,930)

The Official Action has rejected claims 1, 5 – 6, 15 – 18 and 21 – 22 under 35 USC § 102(b) as being anticipated by Jordan (US Patent 4,880,637) (hereafter "Jordan") in light of Orth et al. (US Patent 5,342,930) (hereafter, "Orth"). To the extent that this rejection is a § 102(b) rejection, this rejection is improper. The claimed invention has to be disclosed in a single prior art reference for § 102(b) to apply. The Official Action has failed to establish that either Jordan or Orth alone discloses all the elements of the presently claimed invention.

The Official Action asserts that "Jordan is directed to a method of treatment of a subject infected with a virus comprising the steps of administering a therapeutically effect amount of an NDGA derivative, which may be a water soluble derivative, to a subject," citing NDGA tetrapropionate in Table 7 of the Jordan patent as being "presumed to be a water soluble substituent" (Official Action at page 7). Further, the Official Action asserts that "the complexes of NDGA with zinc chloride or with zinc gluconate are deemed to constitute NDGA derivatives."

Applicants respectfully traverse this § 102(b) rejection and submit that the Official Action has misapplied Jordan or Orth as a § 102(b) reference. Jordan discloses and claims compositions containing catecholic butanes and ionic zinc, the catecholic

butanes having a certain structural formula (see, for example, claim 1 of Jordan at col. 22, line 10). The formula for the catecholic butanes in Jordan is different from the formula for the NDGA derivatives of the present invention (see, for example, claim 1 herein). Since the claimed compositions herein and the Jordan compositions are not identically disclosed, Jordan is not an effective § 102(b) reference. Further, Orth also fails to disclose the NDGA derivatives herein and, thus, also fails as a § 102(b) reference.

Moreover, Applicants disagree with the assertion of the Official Action that NDGA tetrapropionate can be "presumed to be a water soluble substituent." Jordan did not state that NDGA tetrapropionate was water soluble. Applicants do not know whether NDGA tetrapropionate has ever been made and whether NDGA tetrapropionate is water soluble or not. This compound cannot be found in a search of the NCBI database or through an Internet Google search. Jordan certainly did not describe how this compound was to be made. Jordan, therefore is not an enabling prior art reference. Accordingly, the § 102(b) rejection of the present claims over Jordan is improper.

Additionally, Applicants disagree that "complexes of NDGA with zinc chloride or with zinc gluconate" can be "deemed to constitute NDGA derivatives," as asserted in the Official Action. The NDGA derivatives herein are defined by a formula, as shown in claim 1, for example. Any compound or composition that does not meet the requirements of the formula cannot be considered an NDGA derivative, within the context of the present invention.

Even if the Official Action had meant to assert a rejection under 35 USC § 103 instead of § 102, the rejection cannot stand. The Official Action has failed to establish that Jordan discloses all the elements of the presently claimed invention, such as, for example, an NDGA derivative having water-soluble substituents. Further, the Official Action has failed to demonstrate that Orth corrected the deficiencies of Jordan. The combination of Jordan and Orth, therefore, would not have rendered the present invention obvious.

In summary, rejection of claims 1, 5 – 6, 15 – 18 and 21 – 22 is improper under §102(b) as being anticipated by Jordan or Orth. Additionally, the Official Action has failed to carry its burden of establishing that Jordan or Orth discloses or would have

suggested a method for suppressing viral growth, a method of inhibiting replication of an acyclovir-resistant virus, or a method for treatment of such viral infection in a subject, using the compounds as presently claimed in claims 40 (replacing claim1), 5 – 6, 15 – 18 and 21 – 22. Accordingly, rejections under the 35 USC § 102(b) standard over Jordan or Orth is both groundless. Withdrawal of this rejection is requested.

Rejection Under 35 USC §112, First Paragraph

The Official Action has rejected claims 1 – 30 and 39 under 35 USC §112, first paragraph, allegedly on the ground of containing subject matter "which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Official Action asserts that "No basis or support is found in the prior patent for the compound recited in claim 2 and 20, for example, wherein 'N' rather than 'NH' is recited and wherein the dot, is practically illegible in claim 2 and in the wrong position." Claims 2 and 20 have been amended. The present claims do recite "NH" instead of "N." Applicants request withdrawal of this rejection under §112, first paragraph, of these claims.

The Official Action further asserts that "Insertion of the limitation 'are not . . . CH_3O- and $CH_3(C=O)O$-, simultaneously' does not have support in the prior patent. (Official Action at page 4) Applicants submit that the remarks presented above under the heading of "Rejection Under 35 USC § 251" are applicable in this context and, for the same reasons articulated above, the rejected limitation is fully supported by the specification. Applicants request withdrawal of this rejection under 35 USC §112, first paragraph, and favorable consideration of the present claims.

Rejection Under 35 USC §112, Second Paragraph

The Official Action has rejected claims 1 – 30 and 39 under 35 USC §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. The Official Action asserts that "claims 1, 15, 16, 18, for example, are confusing in the recitation of "a formula," and suggested

changing the language to "the formula" (Official Action at page 4). Claim 18 has been canceled and the recitation in claim 18 has been added to claim 17. Claims 40 (replacing claim 1), 15, 16 and 17 now recite "the formula." Rejection of these claims on the ground stated is moot; withdrawal of this rejection under §112, second paragraph, is requested.

Further, the Official Action asserts that claim 1 is vague and indefinite in that the "effective viral growth suppressing amount" to be administered "is not clearly set forth for any and all compounds, any and all viruses and in any and all modes of administration . . ." (Official Action at page 4). Applicants submit that determination of the effective viral growth suppressing amount is within the ordinary skill of a person skilled in the art and need not be specified. It is generally understood within the drug development community that the an effective dose of a therapeutic often depends on the condition of the subject to be treated, the extent of the infection, and sometimes on the age and weight of the subject to be treated, for example, as determined in a clinical trial. It is axiomatic that the patent system does not require clinical trials to be conducted before an applicant can receive a patent on a method of treatment. Applicants' claim 40 (replacing claim 1) is sufficiently clear in specifying that the amount to be administered is the amount that is effective for suppressing viral growth. Hence, a rejection of claim 40 under 35 USC § 112, second paragraph, is without merit. Applicants request withdrawal of this rejection over claim 1.

The Official Action additionally asserts that it is unclear "that substituents per se are 'water soluble.'" Claim 40 (replacing claim 1) recites a formula having R_1, R_2, R_3 and R_4, where each of R_1, R_2, R_3 and R_4 can be one selected from a genus of "water-soluble substituent." Examples of species of the water-soluble substituent are set forth in the specification at, for example, col. 15, line 62 to col. 16, line 25. Applicants submit that metes and bounds of this claim is sufficiently clear to a person of ordinary skill in the art and that it is not necessary for them to provide an exhaustive list of all the species under this genus. Notably, whether a compound having the formula set forth in claim 1 is water soluble or not can be easily determined and does not require undue experimentation. Withdrawal of this rejection is respectfully requested.

The Official Action has rejected claims 5 – 6 and 21 – 22 under 35 USC §112, second paragraph, on the ground that recitation of "inhibited" is confusing. Further, the Official Action recommended that the claims be amended to recite either "the compound" or "the substantially purified compound." Claims 5 – 6 and 21 – 22 have been amended. The stated ground of rejection is not applicable to the present claims. Withdrawal of this rejection is requested.

Moreover, the Official Action has further rejected claim 17 under 35 USC §112, second paragraph, on the ground that it is vague, indefinite and confusing "since it is uncertain how the therapeutically effective amount of a derivative of NDGA is to be determined in a subject 'susceptible to development of resistance to acyclovir," and further asserting that it is uncertain how susceptibility is to be assessed. "There is no clear indication of the timing of the administration, determination of susceptibility, or the identity of the 'derivative' to be administered" (Official Action at page 5). Actually, the previous claim 17 had recited that the "virus is susceptible to development of resistance to acyclovir," not the subject, as asserted in the Official Action. Claim 17 has been amended to recite "treatment of a subject infected with a virus, wherein the virus is resistant to acyclovir," among other things. Tables 5A and 5B show how drug sensitivities were tested. Hence, the rejection of claim 17 under 35 USC §112, second paragraph is inapposite to the present claim. Withdrawal of this rejection is requested.

Double Patenting

The Official Action has rejected claims 1 – 30 and 39 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 -11 of US Patent No. 5,663,209 and claims 24 – 32, 34 – 37 and 40 – 43 of US Patent No. 6,777,444. Further, claims 1 – 30 and 39 stand rejected on the same ground as being unpatentable over claims 1 – 5, 7, and 12 – 14 of US Patent No. 6,214,874 and claims 1 – 9 of US Patent No. 6,417,234, each in view of Shantha (US Patent No. 5,195,965).

Without conceding the merits of the rejections herein, Applicants respectfully request the Examiner to hold this rejection in abeyance until indication of patentability of

the present claims. At the appropriate time, Applicants will file a terminal disclaimer, disclaiming the terminal portion of a patent term.

In light of the foregoing, Applicants submit that the application is in condition for allowance. Applicants request an early indication of allowability of the present claims.

Respectfully submitted,

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